Tandem Ring Opening−Ring Closing Metathesis of Cyclic Olefins

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Abstract: Ruthenium alkylidene **1** has been utilized in the tandem ring opening−ring closing metathesis of cyclic olefins. This reaction produces a bicyclic molecule from a cyclic olefin. Reactivity is dependent upon strain, and thus ring size, in the substrate molecules. Competing oligomerization is observed in substrates having low ring strain; this process is inhibited by increasing dilution of the reaction or by adding alkyl substitution to the acyclic olefins.

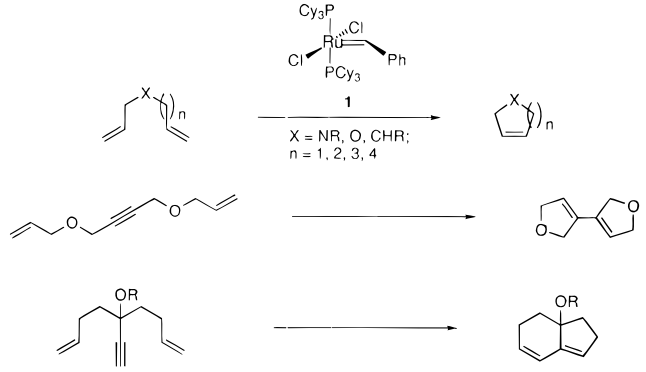
Introduction

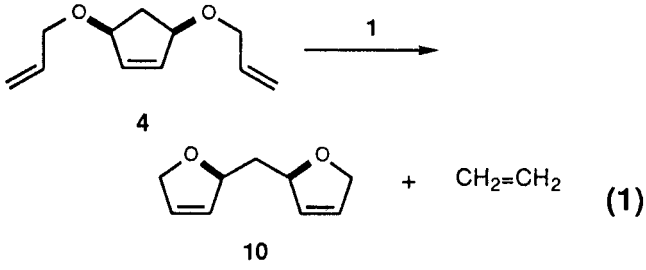
As new catalysts have become more tolerant of functionality and more available, the olefin metathesis reaction has started to play an increasingly significant role in organic synthesis. Many of the applications to date have been ring closing metathesis of dienes. Ruthenium carbene complexes such as **1** effectively catalyze the ring closing metathesis (RCM) of dienes to yield unsaturated carbocycles and heterocycles (Scheme 1).[1] In order to obtain more complex ring systems, it was demonstrated that an acetylene function between the two olefins of the diene acts as a relay, allowing the metathesis catalyst to proceed from one ring to the next to produce a bicyclic product.[2]

In addition to the synthetic utility of RCM, these same metathesis catalysts also promote the ring opening metathesis polymerization (ROMP) of cyclic olefins.[3,4] In ROMP, ring strain is a requisite driving force because the reaction is entropically disfavored. Monomers such as norbornene, cyclobutene, cyclooctene, and cyclopentene are successfully polymerized,[4] while cyclohexenes do not react in this fashion.[5] There are a limited number of cases of cycloheptene ROMP.[6]

The combination of the enthalpically driven ring opening from ROMP and the entropically driven dienyne RCM constitutes a new strategy for the synthesis of organic ring systems. Rather than using an acetylene to relay the metathesis catalyst, this method utilizes the unsaturation of a cycloolefin. A typical substrate molecule (eq 1) has a strained cycloolefin located between olefinic side chains. In analogy to ROMP, this tandem ring opening−ring closing process is enthalpically driven by the reduction in ring strain, and those cyclics which may be successfully polymerized through ROMP represent a starting point for investigations into tandem ring opening−ring closing metathesis. Unlike ROMP, the reaction is entropically driven by the production of ethylene, similar to diene or dienyne RCM, and may proceed if enthalpically neutral or even slightly disfavored.

Scheme 1. Catalytic Ring Closing Metathesis (RCM) of Dienes and Dienynes





(1)

For our initial studies concerning the ring opening−ring closing metathesis of cycloolefins, we have focused on polycyclic ethers. Polycyclic ethers are structural motifs common to many natural and synthetic ionophores, and new methods for their synthesis remain a goal.[7]

[⊗] Abstract published in *Advance ACS Abstracts,* June 15, 1996.

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(2) (a) Kim, S-H.; Bowden, N. B.; Grubbs, R. H. *J. Am. Chem. Soc.* **1994**, *116*, 10801−10802. (b) Kim, S-H.; Zuercher, W. J.; Bowden, N. B.; Grubbs, R. H. *J. Org. Chem.* **1996**, *61*, 1073−1081.

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(4) For general references on ROMP, see: (a) Ivin, K. J. *Olefin Metathesis*; Academic Press: London, 1983. (b) Grubbs, R. H.; Tumas, W. *Science* **1989**, *243*, 907−915. (c) Schrock, R. R. *Acc. Chem. Res.* **1990**, *23*, 158−165. (d) Breslow, D. S. *Prog. Polym. Sci.* **1991**, *18*, 1141−1195.

(5) Cyclohexenes have been found to polymerize under special conditions (*vide infra*). Patton, P. A.; Lillya, C. P.; McCarthy, T. J. *Macromolecules* **1986**, *19*, 1266−1268.

(6) Kress, J. *J. Mol. Catal.* **1995**, *102*, 7−21.

(7) (a) Koert, U. *Synthesis* **1995**, 115−132. (b) Still, W. C.; Cai, D.; Lee, D.; Hauck, P.; Bernardi, A.; Romero, A. *Lectures Heterocycl. Chem.* **1987**, *9*, S33.

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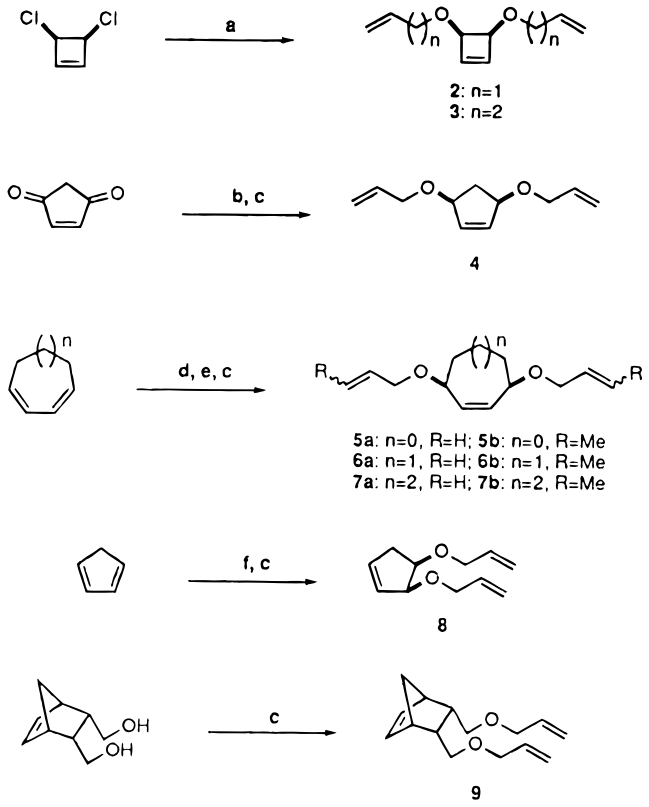
Scheme 2. Synthesis of Ring Opening−Ring Closing Metathesis Cyclic Ether Substrates[a]



[a] (a) NaH, CH_2=$CH(CH_2)_n$OH, 75 °C, 40−66%; (b) $NaBH_4$, $CeCl_3$, MeOH, 58%; (c) NaH, CH_2=$CHCH_2$Br or CH_3CH=$CHCH_2$Br, DMF, 50−80%; (d) $Pd(OAc)_2$(cat), LiOAc, HOAc/pentane, 40−75%; (e) $LiAlH_4$, THF, 75−86%; (f) OsO_4 (cat), tBuOH/H_2O, 89%.

Results and Discussion

Substrate Synthesis. The bis(allyl) ethers of several cycloolefin diols were prepared for the study (Scheme 2). These substrates contain four- to eight-membered rings as well as a norbornene ring system. The cyclobutenes **2** and **3** were obtained by heating a solution of commercially available *cis*-3,4-dichlorocyclobutene and allyl or homoallyl alkoxide in the parent alcohol.[8] Luche reduction[9] of 3,5-cyclopentenedione followed by standard *O*-allylation conditions produced the cyclopentene substrate **4**. Three steps were required to produce **5**−**7**: palladium-catalyzed *cis*-1,4-diacetoxylation,[10] reduction of the acetate to produce the diol, and *O*-alkylation with either allyl or (*E*/*Z*)-crotyl bromide. Osmylation of cyclopentadiene[11] followed by *O*-allylation produced the substrate **8**. The *endo*,*endo*-norbornenediol bis(allyl) ether **9** is made in two steps by reduction of the commercially available anhydride followed by *O*-allylation.

Ring Opening−Ring Closing Metathesis. Treatment of substrates **2**−**9** with 3−6 mol% **1** at slightly elevated temperature afforded the expected bicyclic products in good to excellent yields (Table 1) depending on ring size and reaction concentration. The catalyst efficiently produces dihydrofuran and dihydropyran systems as well as the tricyclic compound **16** which incorporates two oxacycloheptene substructures. Reaction times parallel ring strain energies for the homologous series of cycloolefin starting compounds (entries 1−5):[12] cyclobutene **2** is opened fastest, followed by the five- and eight-membered rings of **4** and **7**. Cycloheptene **6** and cyclohexene **5** appear to be the slowest rings to open.

In contrast to the other ring systems, cyclohexene ROMP has been reported only with heterogeneous catalysts at low temperature or using norbornene as an activator.[5] This failure to polymerize is due to the low ring strain.[13] Similarly, cyclohexene has been ring opened to 1,7-octadiene only at extremely high ethylene pressures.[14] Cyclohexenes were thus expected to be poor relay rings in ring opening−ring closing reactions. These factors, in addition to potential conformational constraints on the intermediate metallacycle, made it questionable at the outset whether the ring would open at a synthetically useful rate, if at all. However, conversion of a six-membered ring to two five-membered rings with concomitant production of ethylene should be thermodynamically favorable due to the entropy change.

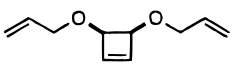
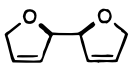
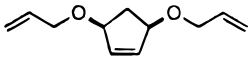
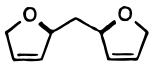
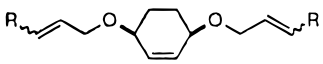
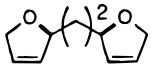
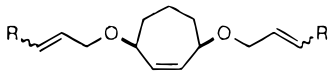
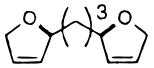
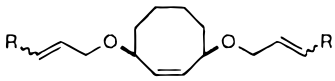
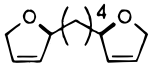
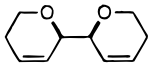
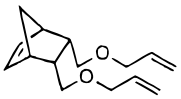
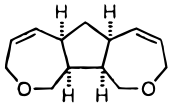
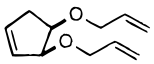
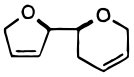
Initial experiments with the six-membered ring relay system suggested that our ring opening−ring closing strategy would be limited to the more strained ring systems. The reactions of **5a**, **6a**, and **7a** yielded multiple products when the reactions were conducted at concentrations near those used for the other substrates. The failure to produce the expected bicyclics was attributed to a competing intermolecular process. Because these processes were not observed in systems having high ring strain (cyclobutene or norbornene), it appeared that the acyclic olefins were reacting via acyclic diene metathesis (ADMET)[15] to produce dimers or other oligomeric species (Scheme 3). Competing intermolecular metathesis has been observed previously for systems in which the rate of cyclization is relatively slower than oligomerization.[16]

The rates of intermolecular metathesis leading to oligomers were effectively decreased relative to the intramolecular reaction leading to the desired bicyclic products by conducting these reactions at higher dilution. For example, the conversion of **5a** to **12** proceeds cleanly and efficiently at 0.008 M in 73% yield (compared to 16% at 0.12 M). A similar dependence of reaction yield on concentration is observed for **6a** and **7a**.

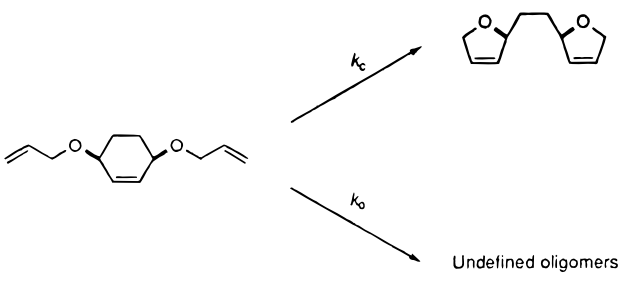
In addition to lowering the concentration, another way to limit the competing intermolecular reactions is to make the acyclic olefins less active for metathesis relative to the cyclic olefin. There is ample precedent that increasing substitution on a particular olefin decreases the rate of olefin metathesis.[2] We reasoned that if the competing oligomerization occurred through metathesis at the acyclic olefins,[17] alkyl substitution would slow this process and allow the metathesis catalyst to react via ring-opening. When the crotyl ethers **5b**−**7b** are reacted with catalyst **1** the reactions proceed in moderate yield at concentrations similar to those used for the other substrates. These yields

(8) Kirmse, W.; Scheidt, F.; Vater, J-J. *J. Am. Chem. Soc.* **1978**, *100*, 3945−3946.
(9) Luche, J.-L. *J. Am. Chem. Soc.* **1978**, *100*, 2226−2227.
(10) Bäckvall, J.-E.; Byström, S. E.; Nordberg, R. E. *J. Org. Chem.* **1984**, *49*, 4619−4631.
(11) Wang, Z-W.; Kakiuchi, K.; Sharpless, K. B. *J. Org. Chem.* **1994**, *59*, 6895−6897.
(12) Greenberg, A.; Liebmann, J. F. *Strained Organic Molecules*; Academic Press: New York, 1978; and references cited therein.
(13) Hocks, L.; Berck, D.; Hubert, A. J.; Teyssie, P. *J. Polym. Sci., Polym. Lett. Ed.* **1975**, *13*, 391−395.
(14) Crain, D. L.; Reusser, A. ACDS Meeting 1972 (New York), Symposium on Advances in Petrochemical Technology.
(15) Wagener, K. B.; Nel, J. G.; Duttweiler, R. P.; Hillmyer, M. A.; Boncella, J. M.; Konzelman, J.; Smith, D. W.; Puts, R.; Willoughby, L. *Rubber Chem. Tech.* **1991**, *64*, 83−95.
(16) (a) Fujimura, O. F.; Fu, G. C.; Grubbs, R. H. *J. Org. Chem.* **1994**, *59*, 4029−4031. (b) Maier, M.E.; Langenbacher, D.; Rebien, F. *Leibigs Ann.* **1995**, 1843−1848. (c) Forbes, M. D. E.; Patton, J. T.; Myers, T. L.; Maynard, H. D.; Smith, D. W., Jr.; Schulz, G. R.; Wagener, K. B. *J. Am. Chem. Soc.* **1992**, *114*, 10978−10980.
(17) Presumably, this is the case because oligomerization is only observed with low strain cycloolefins.

Table 1. Results of Ring Opening−Ring Closing Metathesis Reactions

Entry	Substrate	Product	Yield and Conditions
1	 2	 10	82%, 3 mol % **1**, 0.1 M (C_6H_6), 45°C, 1.5h
2	 4	 11	90%, 5 mol % **1**, 0.1 M (C_6H_6), 60°C, 2h
3a R = H 3b R = Me	 5a, 5b	 12	a: 73%, 0.008 M (C_6H_6),45°C, 6h b: 42%, 6 mol % **1**, 0.2 M (C_6H_6), 45°C, 6h
4a R=H 4b R=Me	 6a, 6b	 13	a: 57%, 0.02 M (C_6H_6), 45°C, 6h b: 56%, 4 mol % **1**, 0.2 M (C_6H_6), 45°C, 6h
5a R=H 5b R=Me	 7a, 7b	 14	a: 85%, 0.01 M (C_6H_6), 45°C, 6h b: 71 %, 6 mol % **1**, 0.1 M (C_6H_6), 45°C, 4h
6	 3	 15	70 %, 3 mol % **1**, 0.07 M (C_6H_6), 45°C, 6h
7	 9	 16	68 %, 6 mol % **1**, 0.04 M (C_6H_6), 45°C, 2h
8	 8	 17	92 %, 5 mol % **1**, 0.04 M (C_6H_6), 60°C, 3h

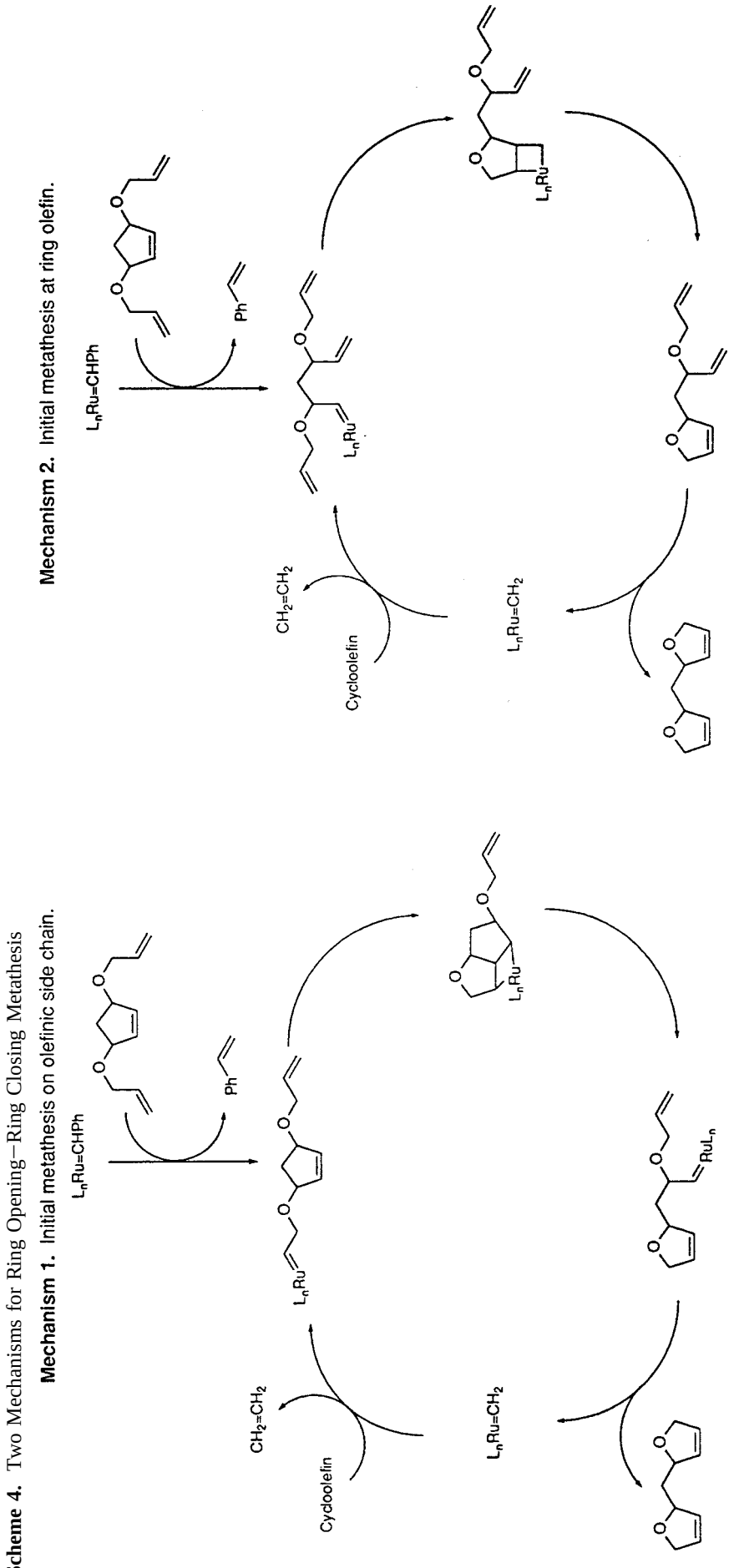
Scheme 3. Competing Processes: Cyclization and Oligomerization



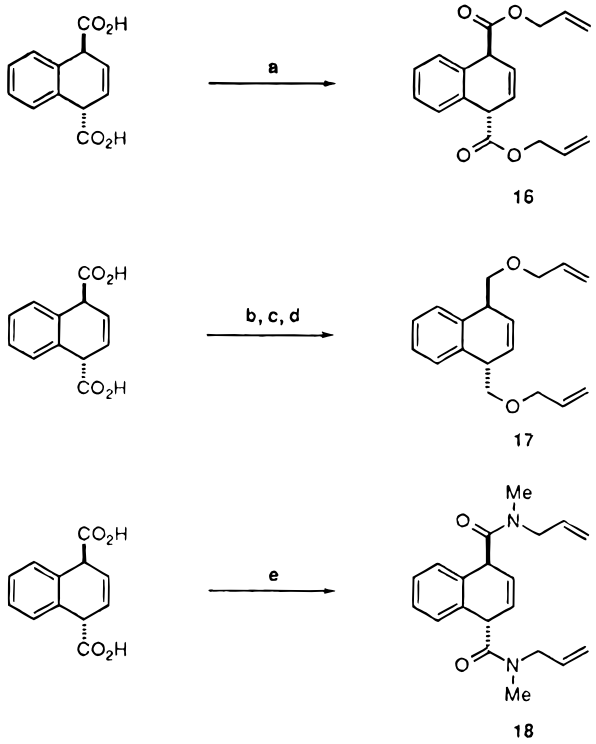
are among the lowest for all of the substrates included in this study, and the mass balance is presumably to be found in a small amount of oligomeric byproducts. The reaction times are somewhat longer than for the other substrates in the homologous series. This observation is consistent with the substitution decreasing the rate of metathesis at the acyclic olefin. Olefin substitution appears to slow the intramolecular process to a lesser extent, and the relative rate of cyclization is effectively increased to allow for product formation.

The observed products are consistent with two mechanisms (Scheme 4). Mechanism 1 involves initial metathesis at the terminal olefin of the allyl group. Productive cleavage of the subsequently formed metallacyclobutane produces the first ring and metal alkylidene. The final step is closure of the ring by an intramolecular olefin metathesis. Mechanism 1 is analogous to the quantitative ring closing metathesis of 1,2-poly(butadi-

Scheme 4. Two Mechanisms for Ring Opening−Ring Closing Metathesis



Scheme 5. Synthesis of *trans*-1,4-Dihydronapthalene-Based Ring Opening−Ring Closing Metathesis Substrates

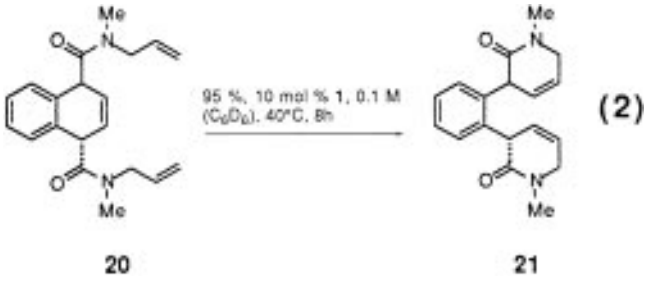


[a] (a) CH_2=$CHCH_2OH$, DCC, CH_2Cl_2, 8%; (b) MeOH, H_2SO_4 (cat), 75%; (c) $LiAlH_4$, Et_2O, 68%; (d) NaH, CH_2=$CHCH_2Br$, DMF, 23%; (e) PCl_5, PhH then $MeNH(CH_2CH$=$CH_2)$.

ene).[18] In mechanism 2 the initial metathesis occurs at the disubstituted cyclic olefin. This step is followed by two diene ring closing steps.

Because increasing olefinic substitution decreases the rate of olefin metathesis, mechanism 1 (initial metathesis at monosubstituted acyclic olefin) is expected to predominate over mechanism 2 (initial metathesis at disubstituted ring olefin). The observed results of dilution and of tether substitution are most consistent with mechanism 1 (*vide supra*). However, mechanism **2** has not been excluded; ring strain may activate the cyclic olefin and favor mechanism 2 in some cases.

To increase the complexity of the system and to further test the utility of cyclohexene systems, a series of compounds based on 1,4-dihydronapthalene was synthesized using standard methods from *trans*-1,4-dihydronapthalene dicarboxylic acid (Scheme 5). Using **1** as catalyst, ester and ether derivatives **18** and **19** fail to ring open, but the *N*-allyl-*N*-methyl amide **20** efficiently produced the tricyclic species **21** (eq 2). A contrast in reactivity of this type between amide and ester was observed previously in the formation of eight-membered rings.[1b] Presumably, **20** is able to undergo ring opening−ring closing metathesis because the favorable conformations of the amide are more energetically accessible than those of the related ether and ester.



Conclusions

We have demonstrated that cyclic unsaturation, similar to acteylenic unsaturation, is an effective relay for olefin metathesis. This relay has been applied in tandem ring opening−ring closing metathesis of four- to eight-membered cycloolefins as well as norbornenes to produce polycyclic ethers. The reactivity as a function of ring size parallels strain energies. Competing intermolecular reactions were observed for rings containing six, seven, and eight members. These intermolecular reactions may be limited by conducting the reaction at high dilution or by increasing the substitution of the olefins involved. Although ring opening reactions involving six-membered rings are not well-known, systems have been presented in which a cyclohexene ring is utilized for a metathesis relay.

Experimental Section

General Methods. High resolution mass spectra were obtained from the Southern California Mass Spectrometry Facility (University of California, Riverside). Analytical thin-layer chromatography (TLC) was performed using silica gel 60 F254 precoated plates (0.25 mm thickness) with a fluorescent indicator. Flash column chromatography was performed using silica gel 60 (230−400 mesh) from EM Science.[19] Catalyst **1** was prepared according to published procedures.[3b] *trans*-1,4-Dihydronapthalene dicarboxylic acid was prepared according to the procedure of Lyssy.[20] The metathesis reactions were carried out under an argon atmosphere with dry, degassed solvents under anhydrous conditions.

***cis*-3,4-Cyclobutenediol Bis(3-butenyl) Ether (3).** To a stirring solution of 3-buten-1-ol (10 mL, 120 mmol) at 0 °C was slowly added NaH (1.3 g, 56 mmol). After allowing the solution to stir for 5 min, *cis*-3,4-dichlorocyclobutene (1.3 g, 10 mmol) was added. The mixture was heated to 75 °C and stirred for 18 h. The reaction was quenched by addition to NH_4Cl (saturated aqueous, 25 mL) and extracted with Et_2O (4 × 25 mL). After concentrating to a dark orange oil, the product was purified on silica gel (10% Et_2O in petroleum ether) to yield **3** (1.25 g, 66%) as a clear, colorless oil: ^{1}H NMR (C_6D_6, 300 MHz) δ 6.08 (d, J = 1.4 Hz, 2H), 5.95−5.81 (m, 2H), 5.11−4.99 (m, 4H), 4.36 (d, J = 1.4 Hz, 2H), 3.58−3.42 (m, 4H), 2.37−2.30 (m, 4H); ^{13}C NMR (C_6D_6, 75 MHz) δ 141.8, 136.0, 116.1, 82.4, 68.2, 35.1; IR (neat, cm^{-1}) 3073, 2953, 2916, 2873, 1111; HRMS calcd for $C_{12}H_{19}O_2$ (MH^+) 195.1385, found 195.1388.

***cis*-3,5-Cyclopentenediol Bis(allyl) Ether (4).** To a stirring solution of *cis*-3,5-cyclopentenediol (600 mg, 6.0 mmol) in DMF (50 mL) at 0 °C was slowly added NaH (420 mg, 18 mmol). After stirring for 1 h, allyl bromide (5.0 mL, 30 mmol) was added, and the reaction mixture was allowed to warm up to room temperature. After 14 h the reaction was partitioned between Et_2O and water (150 mL each) and extracted with Et_2O (4 × 100 mL). After concentrating to a yellow oil, the product was purified on silica gel (10% EtOAc in petroleum ether) to yield **3** (640 mg, 60%) as a clear, colorless oil: ^{1}H NMR (C_6D_6, 300 MHz) δ 5.92−5.77 (m, 4H), 5.00−5.29 (m, 2H), 4.19−4.14 (m, 2H), 3.78−3.87 (m, 4H), 2.40−2.32 (m, 1H), 1.83−1.74 (m, 1H); ^{13}C NMR (C_6D_6, 75 MHz) δ 135.9, 134.6, 115.7, 81.6, 69.4, 38.2; IR (neat, cm^{-1}) 3078, 3014, 2979, 2934, 2855, 1082; HRMS calcd for $C_{11}H_{17}O_2$ (MH^+) 181.1228, found 181.1226.

***meso*-Bis(5-oxa-2-cyclopentenyl)methane (11).** To a vial containing ruthenium catalyst **1** (10 mg, 12 μmol, 3 mol %) in benzene (2 mL) was added ether **4** (65 mg, 360 μmol). The vial was capped and placed in a 45 °C oil bath and stirred 5 h. The reaction mixture was concentrated and purified on silica gel (10% Et_2O in petroleum ether) to yield the product **11** (47 mg, 85%) as a clear, colorless oil: ^{1}H NMR (C_6D_6, 300 MHz) δ 5.64−5.59 (m, 2H), 5.46−5.41 (m, 2H), 5.08−4.96 (m, 2H), 4.52−4.38 (m, 4H), 2.03−1.94 (m, 1H), 1.87−1.78 (m, 1H); ^{13}C NMR (C_6D_6, 75 MHz) δ 130.3, 126.5, 83.4, 74.9, 42.5; IR

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(19) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(20) Lyssy, T. *J. Org. Chem.* **1962**, *27*, 5−13.

(neat, cm^{-1}) 3078, 3014, 2978, 2931, 2854, 1081; HRMS calcd for $C_9H_{13}O_2$ (MH^+) 153.0916, found 153.0915.

***cis*-3,4-Cyclobutenediol Bis(allyl) Ether (2).** Substrate **2** was prepared in a fashion analogous to cyclobutene **3**. **2** was isolated as a clear oil (40%): ^{1}H NMR (C_6D_6, 300 MHz) δ 6.08 (d, J = 0.9 Hz, 2H), 5.95−5.84 (m, 2H), 5.33−5.26 (m, 2H), 5.06−5.00 (m, 2H), 4.42 (d, J = 0.9 Hz, 2H), 4.11−3.94 (m, 4H); ^{13}C NMR (C_6D_6, 75 MHz) δ 141.9, 136.0, 115.6, 81.9, 69.4; IR (neat, cm^{-1}) 3125, 3078, 3051, 3015, 2983, 2861, 1122; HRMS calcd for $C_{10}H_{15}O_2$ (MH^+) 167.1072, found 167.1068.

***meso*-1,1′-Bi(5-oxa-2-cyclopentene) (10).** Bicyclic ether **10** was obtained as a clear, colorless oil (82%) under conditions analogous to the reaction producing **11**: ^{1}H NMR (C_6D_6, 300 MHz) δ 5.81−5.77 (m, 2H), 5.49−5.45 (m, 2H), 4.80−4.76 (m, 2H), 4.52−4.40 (m, 4H); ^{13}C NMR (C_6D_6, 75 MHz) δ 128.2, 127.7, 89.3, 75.8; IR (neat, cm^{-1}) 3079, 2852, 1082; HRMS calcd for $C_8H_{11}O_2$ (MH^+) 139.0759, found 139.0754.

***cis*-3,6-Cyclohexenediol Bis(allyl) Ether (5a).** The ether **5a** was prepared in a manner similar to **4** using allyl bromide, and *cis*-3,6-cyclohexenediol was prepared by the method of Bäckvall. **5a** was isolated as a clear, colorless oil (78%): ^{1}H NMR (C_6D_6, 300 MHz) δ 5.91−5.78 (m, 4H), 5.28−5.20 (m, 2H), 5.05−5.00 (m, 2H), 3.88−3.75 (m, 4H), 3.63−3.59 (m, 2H), 1.91−11.82 (m, 2H), 1.51−1.42 (m, 2H); ^{13}C NMR (C_6D_6, 75 MHz) δ 136.1, 131.0, 115.6, 72.3, 69.2, 25.3; IR (neat, cm^{-1}) 3079, 3031, 2946, 2854, 1086; HRMS calcd for $C_{12}H_{19}O_2$ (MH^+) 195.1385, found 195.1391.

***cis*-3,6-Cyclohexenediol Bis((*E*/*Z*)-2-butenyl) Ether (5b).** The ether **5b** was prepared in a manner similar to **4** using crotyl bromide, and *cis*-3,6-cyclohexenediol was prepared by the method of Bäckvall. **5b** was isolated as a clear, colorless oil (87%): ^{1}H NMR (C_6D_6, 300 MHz) δ 5.93−5.90 (m, 2H), 5.70−5.45 (m, 4H), 3.99−3.79 (m, 4H), 3.69−3.67 (m, 2H), 1.97−1.88 (m, 2H), 1.57−1.44 (m, 8H); ^{13}C NMR (C_6D_6, 75 MHz) δ 131.1, 131.0, 129.1, 128.6, 126.4, 72.2, 71.9, 69.0, 64.0, 25.4, 17.8, 13.2; IR (neat, cm^{-1}) 3027, 2939, 2854, 1092.

***meso*-1,2-Bis(5-oxa-2-cyclopentenyl)ethane (12).** Bicyclic ether **12** was obtained as a clear, colorless oil (73%) under conditions analogous to the reaction producing **10**: ^{1}H NMR (C_6D_6, 300 MHz) δ 5.45−5.40 (m, 4H), 4.84−4.81 (m, 2H), 4.47−4.45 (m, 4H), 1.78−1.56 (m, 4H); ^{13}C NMR (C_6D_6, 75 MHz) δ 130.0, 126.8, 86.2, 75.1, 32.1; IR (neat, cm^{-1}) 3076, 3025, 2930, 1086.

***cis*-3,7-Cycloheptenediol Bis(allyl) Ether (6a).** The ether **6a** was prepared in a manner similar to **4** using allyl bromide, and *cis*-3,7-cycloheptenediol was prepared by the method of Bäckvall. **6a** was isolated as a clear, colorless oil (52%): ^{1}H NMR (C_6D_6, 300 MHz) δ 5.90−5.78 (m, 4H), 5.26 (dd, J = 17.2, 1.7 Hz, 2H), 5.04 (dd, J = 10.4, 1.3 Hz, 2H), 3.88−3.73 (m, 6H), 1.82−1.66 (m, 3H), 1.50−1.29 (m, 3H); ^{13}C NMR (C_6D_6, 75 MHz) δ 135.8, 135.2, 115.6, 79.0, 69.3, 32.9, 25.1; IR (neat, cm^{-1}) 3079, 3015, 2982, 2932, 2856, 1082; HRMS calcd for $C_{13}H_{21}O_2$ (MH^+) 209.1542, found 209.1538.

***cis*-3,7-Cycloheptenediol Bis((*E*/*Z*)-2-butenyl) Ether (6b).** The ether **6b** was prepared in a manner similar to **4** using crotyl bromide, and *cis*-3,7-cycloheptenediol was prepared by the method of Bäckvall. **6b** was isolated as a clear, colorless oil (73%): ^{1}H NMR (C_6D_6, 300 MHz) δ 5.94−5.90 (m, 2H), 5.72−5.45 (m, 4H), 3.98−3.78 (m, 6H), 1.88−1.34 (m, 12H); ^{13}C NMR (C_6D_6, 75 MHz) δ 135.5, 135.4, 128.8, 126.6, 78.9, 78.7, 69.2, 64.2, 33.0, 25.3, 17.8, 13.2; IR (neat, cm^{-1}) 3023, 2933, 2856, 1093.

***meso*-1,3-Bis(5-oxa-2-cyclopentenyl)propane (13).** Bicyclic ether **13** was obtained as a clear, colorless oil (57%) under conditions analogous to the reaction producing **10**: ^{1}H NMR (C_6D_6, 300 MHz) δ 5.47−5.42 (m, 4H), 4.82−4.76 (m, 2H), 4.54−4.42 (m, 4H), 1.65−1.43 (m, 6H); ^{13}C NMR (C_6D_6, 75 MHz) δ 130.2, 126.7, 86.1, 75.0, 36.5, 21.6; IR (neat, cm^{-1}) 3076, 3025, 2930, 1086.

***cis*-3,8-Cyclooctenediol Bis(allyl) Ether (7a).** The ether **7a** was prepared in a manner similar to **4** using allyl bromide, and *cis*-3,8-cyclooctenediol was prepared by the method of Bäckvall. **7a** was isolated as a clear, colorless oil (62%): ^{1}H NMR (C_6D_6, 300 MHz) δ 5.95−5.82 (m, 2H), 5.57−5.54 (m, 2H), 5.27 (dd, J = 17.2, 1.9 Hz, 2H), 5.05 (dd, J = 10.4, 2.0 Hz, 2H), 4.10−3.96 (m, 4H), 3.82−3.74 (m, 2H), 1.94−1.86 (m, 2H), 1.54−1.20 (m, 6H); ^{13}C NMR (C_6D_6, 75 MHz) δ 135.9, 134.3, 115.9, 76.0, 69.6, 36.4, 24.0; IR (neat, cm^{-1}) 3078, 3016, 2982, 29313, 2858, 1082; HRMS calcd for $C_{14}H_{23}O_2$ (MH^+) 223.1698, found 223.1704.

***cis*-3,8-Cyclooctenediol Bis((*E*/*Z*)-2-butenyl) Ether (7b).** The ether **7b** was prepared in a manner similar to **4** using crotyl bromide and, *cis*-3,8-cyclooctenediol was prepared by the method of Bäckvall. **7b** was isolated as a clear, colorless oil (74%): ^{1}H NMR (C_6D_6, 300 MHz) δ 5.74−5.47 (m, 6H), 4.17−3.96 (m, 4H), 3.84−3.91 (m, 2H), 1.99−1.89 (m, 2H), 1.56−1.18 (m, 18H); ^{13}C NMR (C_6D_6, 75 MHz) δ 134.3, 134.2, 134.1, 128.6, 127.6, 126.4, 75.6, 75.3, 69.1, 36.3, 36.2, 23.8, 17.5; IR (neat, cm^{-1}) 3018, 2932, 2857, 1095; HRMS calcd for $C_{16}H_{27}O_2$ (MH^+) 251.2011, found 251.2013.

***meso*-1,4-Bis(5-oxa-2-cyclopentenyl)butane (14).** Bicyclic ether **14** was obtained as a clear, colorless oil (71%) under conditions analogous to the reaction producing **10**: ^{1}H NMR (C_6D_6, 300 MHz) δ 5.48−5.43 (m, 4H), 4.80−4.77 (m, 2H), 4.52−4.44 (m, 2H), 1.54−1.32 (m, 8H) ^{13}C NMR (C_6D_6, 75 MHz) δ 130.2, 126.7, 86.1, 75.0, 36.5, 25.8; IR (neat, cm^{-1}) 3077, 2932, 2853, 1078; HRMS calcd for $C_{12}H_{19}O_2$ (MH^+) 195.1385, found 195.1383.

***cis*-3,4-Cyclopentenediol Bis(allyl) Ether (8).** The ether **8** was prepared in a manner similar to **4** using allyl bromide, and *cis*-3,4-cyclopentenediol was prepared by the method of Sharpless from cyclopentadiene. **8** was isolated as a clear, colorless oil (52%): ^{1}H NMR (C_6D_6, 300 MHz) δ 5.99−5.83 (m, 2H), 5.74−5.70 (m, 1H), 5.66−5.63 (m, 1H), 5.35−5.25 (m, 2H), 5.06−5.01 (m, 2H), 4.20−3.77 (m, 6H), 2.46−2.38 (m, 1H), 2.23−2.15 (m, 1H); ^{13}C NMR (C_6D_6, 75 MHz) δ 136.4, 135.9, 133.5, 130.2, 115.6, 115.4, 80.4, 79.0, 70.8, 69.7, 37.0; IR (neat, cm^{-1}) 3077, 3014, 2982, 2917, 2855, 1124; HRMS calcd for $C_{11}H_{17}O_2$ (MH^+) 181.1228, found 181.1238.

4-(5-Oxa-2-cyclopentenyl)-5-oxacyclohexene (17). Bicyclic ether **15** was obtained as a clear, colorless oil (92%) under conditions analogous to the reaction producing **10**: ^{1}H NMR (C_6D_6, 300 MHz) δ 5.88−5.84 (m, 1H), 5.66−5.60 (m, 1H), 5.51−5.48 (m, 1H), 5.41−5.36 (m, 1H), 4.84−4.81 (m, 1H), 4.48−4.43 (m, 2H), 4.03−3.96 (m, 2H), 3.47−3.40 (m, 1H), 2.18−2.00 (m, 2H); ^{13}C NMR (C_6D_6, 75 MHz) δ 127.8, 127.7, 126.6, 124.1, 88.8, 76.6, 75.7, 65.8, 27.7; IR (neat, cm^{-1}) 3035, 2919, 2848, 1090; HRMS calcd for $C_9H_{13}O_2$ (MH^+) 153.0916, found 153.0916.

***meso*-1,1′-Bi(6-oxa-2-cyclohexene) (15).** Bicyclic ether **15** was obtained as a clear, colorless oil (70%) under conditions analogous to the reaction producing **10**: ^{1}H NMR (C_6D_6, 300 MHz) δ 5.76−5.69 (m, 2H), 4.13 (s, 2H), 3.85−3.78 (m, 2H), 3.47−3.38 (m, 2H), 2.07−1.98 (m, 2H), 1.56−1.47 (m, 2H); ^{13}C NMR (C_6D_6, 75 MHz) δ 128.4, 125.5, 76.4, 63.5, 25.6; IR (neat, cm^{-1}) 3040, 2960, 2918, 2852, 1091; HRMS calcd for $C_{10}H_{15}O_2$ (MH^+) 167.1080, found 167.1072.

***endo,endo*-5,6-Bis(2-oxa-4-pentenyl)bicyclo[2.2.1]hept-2-ene (9).** The ether **9** was prepared in a manner similar to **4** using allyl bromide and *endo,endo*-5-norbornene-2,3-dimethanol. **9** was isolated as a clear, colorless oil (55%): ^{1}H NMR (C_6D_6, 300 MHz) δ 6.09−6.08 (m, 2H), 5.91−5.78 (m, 2H), 5.28−5.20 (m, 2H), 5.06−5.01 (m, 2H), 3.78−3.73 (m, 4H), 3.27−3.22 (m, 2H), 3.02−2.93 (m, 4H), 2.52−2.46 (m, 2H), 1.50−1.46 (m, 1H), 1.18−1.14 (m, 1H); ^{13}C NMR (C_6D_6, 75 MHz) δ 135.9, 135.5, 115.8, 71.9, 70.7, 49.3, 46.1, 42.0; IR (neat, cm^{-1}) 3059, 2961, 2919, 2864, 1092; HRMS calcd for $C_{15}H_{23}O_2$ (MH^+) 235.1698, found 235.1698.

***cis,cis*-5,10-Dioxatricyclo[8.5.0.0^{8,14}]pentadeca-2,12-diene (16).** Tricyclic ether **14** was obtained as a clear, colorless oil (68%) under conditions analogous to the reaction producing **10**: ^{1}H NMR (C_6D_6, 300 MHz) δ 5.46−5.39 (m, 2H), 5.17−5.11 (m, 2H), 4.16−4.08 (m, 2H), 3.95−3.74 (m, 2H), 3.46−3.39 (m, 2H), 2.53−2.36 (m, 4H), 1.92−1.84 (m, 1H), 1.37−1.26 (m, 2H); ^{13}C NMR (C_6D_6, 75 MHz) δ 130.8, 127.1, 71.2, 69.6, 47.5, 42.1, 41.9; IR (neat, cm^{-1}) 3003, 2928, 2873, 2817, 1124; HRMS calcd for $C_{13}H_{19}O_2$ (MH^+) 207.1385, found 207.1375.

Diallyl *trans*-1,4-Dihydronapthalene 1,4-Dicarboxylate (18). To a stirring solution of *trans*-1,4-dihydronapthalene 1,4-dicarboxylic acid (655 mg, 3 mmol) and allyl alcohol (0.48 mL, 7 mmol) in CH_2Cl_2 (15 mL) at ambient temperature was added DCC (1.4 g, 7 mmol). The reaction mixture was allowed to stir 12 h. After purification on silica gel (CH_2Cl_2 elution) the product **18** (70 mg, 8%) was isolated as a white crystalline solid: ^{1}H NMR (C_6D_6, 300 MHz) δ 7.25−7.22 (m, 2H), 7.05−7.02 (m, 2H), 6.01−5.99 (m, 2H), 5.67−5.54 (m, 2H), 5.02−4.86 (m, 4H), 4.35−4.32 (m, 4H), 4.22−4.21 (m, 2H); ^{13}C NMR

($CDCl_3$, 75 MHz) δ 135.8, 134.8, 127.7, 126.3, 123.5, 116.7, 75.4, 72.0, 39.3; IR (neat, cm^{-1}) 3082, 3027, 2983, 2936, 2886, 2864, 1732, 1119; HRMS calcd for $C_{18}H_{22}NO_4$ (MNH_4^+) 316.1549, found 316.1563.

***trans*-1,4-Bis(2-oxa-4-pentenyl)-1,4-dihydronapthalene (19).** To a stirring solution of *trans*-1,4-dihydronapthalene-1,4-dimethanol in DME was added NaH. After 30 min, allyl bromide was added, and stirring was continued for 2 h. The reaction was quenched with 1.0 N HCl (20 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The extracts were combined, concentrated *in vacuo*, and purified on silica gel to yield **19** (320 mg, 23%) as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.38−7.34 (m, 2H), 7.25−7.20 (m, 2H), 6.10 (s, 2H), 5.96−5.85 (m, 2H), 5.32−5.16 (m, 4H), 4.03−3.98 (m, 4H), 3.74−3.50 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 135.8, 134.8, 127.7, 126.3, 123.5, 75.4, 72.0, 39.3; IR (neat, cm^{-1}) HRMS calcd for $C_{18}H_{26}NO_2$ (MNH_4^+) 288.1963, found 288.1972.

***N,N′*-Diallyl-*N,N′*-dimethyl-*trans*-1,4-dihydronapthalene 1,4-Dicarboxamide (20).** A solution containing *trans*-1,4-dihydronapthalene dicarboxylic acid (500 mg, 2.3 mmol) and PCl_5 (1.0 g, 4.8 mmol) in benzene (50 mL) was heated to reflux for 2 h. The reaction mixture was then cooled, and the benzene was removed *in vacuo*. The residue was dissolved in a minimum amount of CH_2Cl_2 and passed through a plug of silica gel. The solution was again concentrated, and the residue was dissolved in CH_2Cl_2 along with *N*-methylallylamine (0.64 mL, 4.6 mmol) and triethylamine (0.44 mL, 3.1 mmol). The reaction mixture was stirred 12 h and then quenched with 1.0 N HCl and extracted with Et_2O (3 × 30 mL). The diamide **20** (140 mg, 19%) was isolated as a white crystalline solid after recrystallization from Et_2O/petroleum ether: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.26−7.12 (m, 4H), 6.13−6.08 (m, 2H), 5.78−5.64 (m, 2H), 5.23−5.12 (m, 4H), 4.88−4.78 (m, 2H), 4.02−4.01 (m, 4H), 2.95 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.2, 172.6, 132.7, 127.4, 127.2, 126.0, 125.8, 125.7, 117.4, 117.2, 52.4, 50.7, 45.8, 45.6, 45.2, 45.0, 34.9, 34.0; IR (neat, cm^{-1}) 3078, 2981, 2930, 1636; HRMS calcd for $C_{20}H_{25}N_2O_2$ (MH^+) 325.1916, found 325.1904.

1,2-Bis(*N*-methyl-2-cyclohexamid-3-enyl)benzene (21). Tricyclic amide **21** was obtained from **20** as a clear oil (95%) under conditions analogous to the reaction producing **10**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.16−7.14 (m, 4H), 6.08−6.02 (m, 2H), 5.96−5.90 (m, 2H), 5.15−5.11 (m, 2H), 4.17−3.96 (m, 4H), 2.99 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 169.0, 139.8, 128.2, 127.9, 127.1, 120.2, 51.2, 43.0, 34.3; IR (neat, cm^{-1}) 3048, 2920, 1639; HRMS calcd for $C_{18}H_{21}N_2O_2$ (MH^+) 297.1603, found 297.1605.

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Supporting Information Available: ^{1}H NMR spectra of compounds **2**−**21** (25 pages). See any current masthead page for ordering and Internet access instructions.

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